Food and Drug Administration (FDA)
Center for Drug Evaluation and Research (CDER)
Joint Meeting of the Drug Safety and Risk Management Advisory Committee, Nonprescription Drugs Advisory Committee, and the Anesthetic and Life Support Drugs Advisory Committee
June 29-30, 2009

Questions to the Committee

For each question, the relevant Option from the background package's Options Paper is presented in a text box. Although the order of presentation has been changed, these options are numbered as they appear in the Options Paper.

A set of General Considerations for you to take into account in your discussion and decisions of all questions is provided on Page 9. In addition, other factors that you should take into account are listed and you may identify other factors that you find relevant.

Nonprescription Products

FROM OPTIONS PAPER: "OPTION 1a"

Reduce the current dosage strengths of acetaminophen in nonprescription products. This could include the maximum adult daily dose, maximum single adult dose, and maximum dosage strength.

In addition to the General Considerations, consider the following:

- Efficacy provided by the higher single and daily doses
- Availability of different doses for various clinical indications
- Additional safety concerns posed by the availability of higher strength acetaminophen products compared to lower strength products
- Balance of efficacy benefit with safety concerns
- How the "best" dosage should be determined
- FDA will consider responses to Questions 1 and 2 when determining whether to reduce the current dosage strengths of acetaminophen in prescription products.

Question 1 (Vote)

Do you recommend that the maximum total daily dose (4 grams/day) of acetaminophen in nonprescription single ingredient and combination products be lowered?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

Question 2 (Vote)

Do you recommend that the maximum nonprescription single adult dose be limited to 650 mg?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

FROM OPTIONS PAPER: “OPTION 1b”

If OTC dose were reduced, switch of current higher dosage to prescription status. This could be 500 mg per tablet, 1000 mg per maximum dose and/or 4 grams as the maximum daily dose.

In addition to the General Considerations, consider the following:

- Patient population(s) under healthcare providers’ care who may require the current maximum strength of acetaminophen

Question 3 (Vote)

If the current doses of nonprescription products are lowered, do you recommend that the current maximum dosage of acetaminophen (i.e., 2 x 500 mg) be switched to prescription status?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

FROM OPTIONS PAPER: “OPTION 2”

Establish pack size limits for OTC acetaminophen products.

In addition to General Considerations, consider the following:

- The impact of the U.K. experience with mandated pack size restriction and no mandated sales restriction
- Relevance of the U.K. experience to the U.S. marketplace
- How FDA should determine an appropriate OTC pack size
- Public health and safety consequences of the potential for increased use of other analgesics

Question 4 (Vote)

Do you recommend that pack size limits be implemented for nonprescription acetaminophen products?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

FROM OPTIONS PAPER: “OPTION 5a”

Eliminate nonprescription acetaminophen combination products.

In addition to the General Considerations, consider the following:

- Role of combination products in duplicate dosing of acetaminophen
- Consumer knowledge about presence of acetaminophen in OTC combination products

Question 5 (Vote)

Do you recommend eliminating nonprescription acetaminophen combination products?
A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

FROM OPTIONS PAPER: “OPTION 6”

Limit formulations for OTC LIQUIDS.

In addition to the General Considerations, consider the following:

- The OTC monograph does not currently stipulate specific concentrations of acetaminophen liquid formulations
- Dosage administration considerations for pediatric patients of various ages
- Identifying the concentration of acetaminophen liquid that should be made available for children, if only one concentration is allowed

Question 6 (Vote)

Do you recommend that only one concentration of nonprescription acetaminophen liquid be available?
A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

Prescription Products

FROM OPTIONS PAPER: “OPTION 5b”

Eliminate prescription acetaminophen combination products.

In addition to the General Considerations, consider the following:

- Currently, the combination products fall under Schedule III. Single ingredient opioid analgesics, by DEA regulation, are regulated as Schedule II and have different prescribing and dispensing requirements.
- Potential safety concerns associated with the drugs that will be used as therapeutic replacements for the opioid-acetaminophen combinations (e.g., NSAIDs, Schedule II opioids.)

Question 7 (Vote)

Do you recommend eliminating the prescription acetaminophen combination products?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

FROM OPTIONS PAPER: “OPTION 3” and “OPTION 4”

If prescription acetaminophen combination products continue to be marketed, implement additional safety measures by requiring “unit-of-use” packaging and/or additional warning materials.

With “unit-of-use” packaging, products would be packaged by the manufacturer or distributer for sale in a pharmacy, without the product needing to be repackaged. Packaging would display standardized information on the prescription package directed to patients (e.g., prominent display of ‘ACETAMINOPHEN’ as an active ingredient and a warning about potential liver damage.) and convey a Medication Guide to patients.

A boxed warning could be implemented with or without “unit-of-use” packaging.

In addition to the General Considerations, consider the following:

- FDA recently issued new regulations for labeling OTC products containing acetaminophen to enhance warning information and prominence of identification of ‘acetaminophen’ as an active ingredient.
- Current pharmacy practices do not require consistent nomenclature and warning information on pharmacy-packaged prescriptions.

Question 8 (Vote)

If prescription acetaminophen combination products continue to be marketed, do you recommend that “unit-of-use” packages be required?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

Question 9 (Vote)

Do you recommend that FDA require a boxed warning for prescription acetaminophen combination products?

A – Yes, I recommend this change and consider it a high priority
B – Yes, I recommend this change
C – No, I do not recommend this change

Question 10 (Vote)

Overall Ranking of Options

Options related to both Rx and OTC products containing acetaminophen have been discussed. You have already indicated whether you consider each individual option a high priority. To further clarify how FDA should focus its resources to decrease the public health burden of acetaminophen liver toxicity, indicate the single option, including both nonprescription and prescription options, which you recommend that FDA consider its highest priority. If you do not recommend that FDA implement any of the proposed options, please indicate this on the ballot provided.

Nonprescription Products

Option 1a - Reduce maximum dose of OTC acetaminophen
Option 1b – Switch current maximum dose of OTC acetaminophen to prescription
Note: Options 1a and 1b may be considered a single option or two separate options.

Option 2 - Establish pack size limits for OTC products

Option 5a – Eliminate OTC acetaminophen combination products.

Option 6 - Limit OTC liquid formulations

Prescription Products

Option 5b - Eliminate prescription acetaminophen combination products

Option 3 - Require unit of use packaging for prescription acetaminophen combination products

Option 4 - Require a boxed warning for prescription acetaminophen combination products

Question 11 (Discuss)

What other options FDA should consider that have not been discussed in the options provided?

The ‘General Considerations’ apply to each of the questions. You may want to tear off this sheet and use it for reference when responding.

General Considerations

- Potential for this change to decrease incidence of liver injury
- Effect on patients (e.g., convenience, monetary factors, education)
- Effect on healthcare practitioners
- Whether the regulatory steps, resources, and time needed to implement this change are merited by the potential impact of the change
- Steps that manufacturers would need to take to support this change
- Other potential consequences of this change that should be anticipated

Committee Vote

Note: the following abbreviations are used:

CR: Consumer Representative
PR: Patient Representative

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Question 1

Vote Result

Presented	**37**
Yes, High Priority	**11**
Yes	**10**
No	**16**
No-Voting	**0**

Vote Time: 2009-06-30 11:50:55

Name List

Proposal Name:

Question 1

Yes, High Priority (Vote: 11)

Chojkier	DeNisco	Eichner (PR)
Gellad	Heckbert	Olsen
Omogui (CR)	Shrank	Stergachis
Walker-Harding	Wolfe (CR)	

Yes (Vote: 10)

Cooper	Day	Eisenach
Farber	Griffin	Kirsch
Kramer	Lorenz	Pollock
Watts		

No (Vote: 16)

Benowitz	Brull	Covington
Engle	Kerns	Krenzelok
Landis	Levine	Markman
Morrato	Nelson (Chair)	Prough
Raja	Todd	Vaida
Zelterman		

No-Voting (Total: 0)

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Question 2

Vote Result

Presented	**37**
Yes, High Priority	**12**
Yes	**12**
No	**13**
No-Voting	**0**

Vote Time: 2009-06-30 11:53:30

Name List

Proposal Name:

Question 2

Yes, High Priority (Vote: 12)

DeNisco	Eichner (PR)	Eisenach
Farber	Gellad	Heckbert
Kramer	Lorenz	Olsen
Omogui (CR)	Stergachis	Wolfe (CR)

Yes (Vote: 12)

Benowitz	Chojkier	Cooper
Covington	Day	Griffin
Kirsch	Pollock	Raja
Shrank	Walker-Harding	Watts

No (Vote: 13)

Brull	Engle	Kerns
Krenzelok	Landis	Levine
Markman	Morrato	Nelson (Chair)
Prough	Todd	Vaida
Zelterman		

No-Voting (Total: 0)

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Question 3

Vote Result

Presented	**37**
Yes, High Priority	**8**
Yes	**18**
No	**11**
No-Voting	**0**

Vote Time: 2009-06-30 12:09:03

Name List

Proposal Name:

Question 3

Yes, High Priority (Vote: 8)

Benowitz	DeNisco	Heckbert
Kramer	Lorenz	Omogui (CR)
Shrank	Watts	

Yes (Vote: 18)

Chojkier	Cooper	Covington
Day	Eichner (PR)	Eisenach
Farber	Gellad	Griffin
Morrato	Nelson (Chair)	Olsen
Prough	Raja	Stergachis
Todd	Vaida	Walker-Harding

No (Vote: 11)

Brull	Engle	Kerns
Kirsch	Krenzelok	Landis
Levine	Markman	Pollock
Wolfe (CR)	Zelterman	

No-Voting (Total: 0)

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Question 4

Vote Result

Presented	**37**
Yes, High Priority	**2**
Yes	**15**
No	**20**
No-Voting	**0**

Vote Time: 2009-06-30 13:33:11

Name List

Proposal Name:

Question 4

Yes, High Priority (Vote: 2)

Morrato	Olsen	

Yes (Vote: 15)

Chojkier	Day	DeNisco
Eichner (PR)	Eisenach	Kramer
Landis	Levine	Markman
Shrank	Stergachis	Vaida
Walker-Harding	Wolfe (CR)	Zelterman

No (Vote: 20)

Benowitz	Brull	Cooper
Covington	Engle	Farber
Gellad	Griffin	Heckbert
Kerns	Kirsch	Krenzelok
Lorenz	Nelson (Chair)	Omogui (CR)
Pollock	Prough	Raja
Todd	Watts	

No-Voting (Total: 0)

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Question 5

Vote Result

Presented	**37**
Yes, High Priority	**2**
Yes	**11**
No	**24**
No-Voting	**0**

Vote Time: 2009-06-30 13:55:17

Name List

Proposal Name:

Question 5

Yes, High Priority (Vote: 2)

Farber	Kramer	

Yes (Vote: 11)

Chojkier	Day	DeNisco
Eichner (PR)	Krenzelok	Levine
Morrato	Nelson (Chair)	Todd
Walker-Harding	Wolfe (CR)	

No (Vote: 24)

Benowitz	Brull	Cooper
Covington	Eisenach	Engle
Gellad	Griffin	Heckbert
Kerns	Kirsch	Landis
Lorenz	Markman	Olsen
Omogui (CR)	Pollock	Prough
Raja	Shrank	Stergachis
Vaida	Watts	Zelterman

No-Voting (Total: 0)

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Question 6

Vote Result

Presented	**37**
Yes, High Priority	**19**
Yes	**17**
No	**1**
No-Voting	**0**

Vote Time: 2009-06-30 14:17:38

Name List

Proposal Name:

Question 6

Yes, High Priority (Vote: 19)

Brull	Cooper	DeNisco
Eichner (PR)	Eisenach	Griffin
Heckbert	Levine	Lorenz
Nelson (Chair)	Olsen	Pollock
Prough	Shrank	Stergachis
Vaida	Walker-Harding	Watts
Wolfe (CR)		

Yes (Vote: 17)

Benowitz	Chojkier	Covington
Day	Engle	Farber
Gellad	Kerns	Kirsch
Kramer	Landis	Markman
Morrato	Omogui (CR)	Raja
Todd	Zelterman	

No (Vote: 1)

Krenzelok

No-Voting (Total: 0)

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Question 7

Vote Result

Presented	**37**
Yes, High Priority	**10**
Yes	**10**
No	**17**
No-Voting	**0**

Vote Time: 2009-06-30 14:52:47

Name List

Proposal Name:

Question 7

Yes, High Priority (Vote: 10)

Chojkier	Cooper	DeNisco
Eisenach	Farber	Heckbert
Levine	Nelson (Chair)	Vaida
Wolfe (CR)		

Yes (Vote: 10)

Benowitz	Covington	Day
Eichner (PR)	Kirsch	Kramer
Shrank	Stergachis	Watts
Zelterman		

No (Vote: 17)

Brull	Engle	Gellad
Griffin	Kerns	Krenzelok
Landis	Lorenz	Markman
Morrato	Olsen	Omogui (CR)
Pollock	Prough	Raja
Todd	Walker-Harding	

No-Voting (Total: 0)

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Question 8

Vote Result

Presented	**37**
Yes, High Priority	**5**
Yes	**22**
No	**10**
No-Voting	**0**

Vote Time: 2009-06-30 15:38:35

Name List

Proposal Name:

Question 8

Yes, High Priority (Vote: 5)

Benowitz	Heckbert	Levine
Markman	Prough	

Yes (Vote: 22)

Brull	Chojkier	Cooper
Covington	Day	DeNisco
Eichner (PR)	Eisenach	Farber
Griffin	Kerns	Kramer
Landis	Morrato	Nelson (Chair)
Olsen	Pollock	Raja
Stergachis	Todd	Walker-Harding
Wolfe (CR)		

No (Vote: 10)

Engle	Gellad	Kirsch
Krenzelok	Lorenz	Omogui (CR)
Shrank	Vaida	Watts
Zelterman		

No-Voting (Total: 0)

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Question 9

Vote Result

Presented	**37**
Yes, High Priority	**25**
Yes	**11**
No	**1**
No-Voting	**0**

Vote Time: 2009-06-30 15:39:55

Name List

Proposal Name:

Question 9

Yes, High Priority (Vote: 25)

Benowitz	Brull	Chojkier
Cooper	Day	DeNisco
Eichner (PR)	Eisenach	Engle
Gellad	Heckbert	Kramer
Levine	Markman	Morrato
Olsen	Omogui (CR)	Prough
Raja	Shrank	Stergachis
Walker-Harding	Watts	Wolfe (CR)
Zelterman		

Yes (Vote: 11)

Covington	Farber	Kerns
Kirsch	Krenzelok	Landis
Lorenz	Nelson (Chair)	Pollock
Todd	Vaida	

No (Vote: 1)

Griffin

No-Voting (Total: 0)

Question 10 Vote Record

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OPTION		NONPRESCRIPTION PRODUCTS						PRESCRIPTION PRODUCTS			Do Not Recommend that FDA implement any of the proposed options.
Sheet #	Name	1	1a	1b	2	5a	6	5b	3	4	X
1	Benowitz		1								
2	Brull									1	
3	Chojkier							1			
4	Cooper						1				
5	Covington							1			
6	Day		1								
7	DeNisco	1									
8	Eichner	1									
9	Eisenach							1			
10	Engle									1	
11	Farber							1			
12	Gellad	1									
13	Griffin								1		
14	Heckbert	1									
16	Kerns						1				
17	Kirsch							1			
18	Kramer							1			
19	Krenzelok									1	
20	Landis									1	
21	Levine					1					
22	Lorenz	1									
23	Markman									1	
24	Morrato									1	
25	Nelson, L (Chair)						1				
26	Olsen		1								
27	Omoigui	1									
28	Pollock						1				
29	Prough									1	
30	Raja			1							
31	Shrank	1									
32	Stergachis	1									
33	Todd					1					
34	Vaida							1			
35	Walker-Harding						1				
36	Watts						1				
37	Wolfe	1									
38	Zelterman						1				
	TOTALS	9	3	1	0	2	7	7	1	7	0
	OPTION	1	1a	1b	2	5a	6	5b	3	4	X